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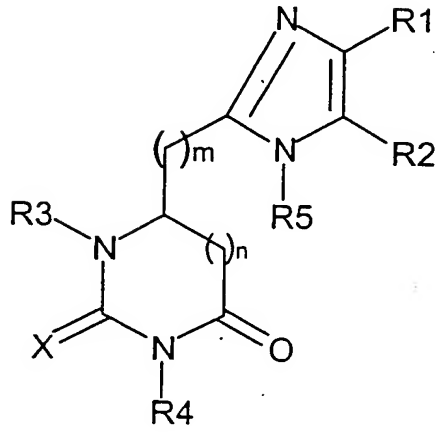
Claims

1. Compound of general formula **(I)** represented below



(I)

in racemic, enantiomeric form or all combinations of these forms, in which:

R1 represents a $(C_1\text{-}C_{12})$alkyl, $(C_0\text{-}C_6)$alkyl-C(O)-O-Z1, $(C_0\text{-}C_6)$alkyl-C(O)-NH-$(CH_2)_p$-Z2 or aryl radical optionally substituted,

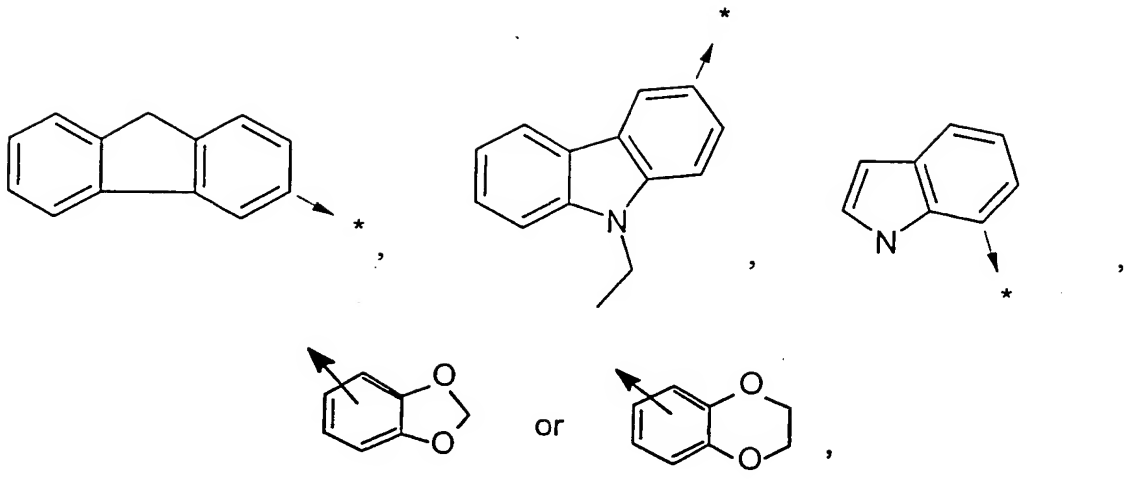
Z1 represents H, a $(C_1\text{-}C_6)$ alkyl, -$(CH_2)_p$-aryl radical;

Z2 represents an amino, $(C_1\text{-}C_{12})$alkylamino, $(C_3\text{-}C_8)$cycloalkylamino, N,N-di-$(C_1\text{-}C_{12})$alkylamino, NH-C(O)-O-$(CH_2)_p$-phenyl, NH-C(O)-O-$(CH_2)_p$-$(C_1\text{-}C_6)$alkyl radical, an optionally substituted carbocyclic or heterocyclic aryl radical or an optionally substituted heterocyclic non aromatic radical;

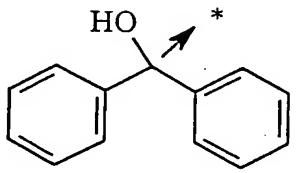
R2 represents H, $(C_1\text{-}C_{12})$alkyl or aryl optionally substituted;

R3 represents H or $(CH_2)_p$–Z3;

Z3 represents $(C_1\text{-}C_{12})$alkyl, $(C_1\text{-}C_{12})$alkenyl, $(C_3\text{-}C_8)$cycloalkyl, Y1-$(CH_2)_p$-phenyl-$(X1)_n$, -S-$(C_1\text{-}C_{12})$alkyl, S-$(C_1\text{-}C_{12})$alkyl-S-S-$(C_1\text{-}C_{12})$alkyl, an optionally substituted carbocyclic or heterocyclic aryl radical, and in particular one of the radicals represented below

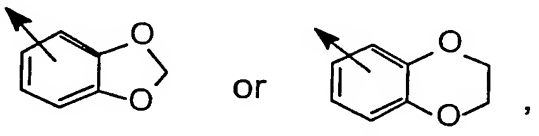


an optionally substituted heterocyclic non aromatic radical, a *bis*-arylalkyl or di-arylalkyl radical or also the radical



Y1 represents O, S, NH or is absent;

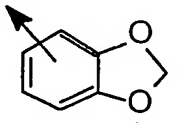
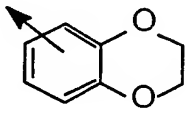
R4 represents $(CH_2)_p$–Z4;
Z4 represents amino, $(C_1$-$C_{12})$alkyl, $(C_3$-$C_8)$cycloalkyl, $(C_1$-$C_{12})$alkylamino, N,N-di-$(C_1$-$C_{12})$alkylamino, amino$(C_3$-$C_6)$cycloalkyl, amino$(C_1$-$C_6)$alkyl$(C_3$-$C_6)$cycloalkyl$(C_1$-$C_6)$alkyl, carbocyclic or heterocyclic aminoaryl, $(C_1$-$C_{12})$alkoxy, $(C_1$-$C_{12})$alkenyl, N-C(O)O$(C_1$-$C_6)$alkyl, an optionally substituted carbocyclic or heterocyclic aryl radical, an optionally substituted heterocyclic non aromatic radical, *bis*-arylalkyl, di-arylalkyl or one of the radicals represented below



or also Z4 represents an N(R6)(R7) radical in which R6 and R7 taken together with the nitrogen atom which they carry form together a heterocycle with 5 to 7 members;

R5 represents H, -$(CH_2)_p$-C(O)-$(CH_2)_p$-Z5, -$(CH_2)_p$-Z5, -$(CH_2)_p$-OZ5 or -$(C_0$-$C_6)$alkyl-C(O)-NH-$(CH_2)_p$-Z5,

Z5 representing an optionally substituted radical chosen from the group constituted by the -(C_1-C_{12})alkyl, benzo[b]thiophene, phenyl, naphthyl, benzo[b]furannyl, thiophene, isoxazolyl, indolyl radicals, and

 or  ;

it being understood that an optionally substituted radical or an optionally substituted phenyl is optionally substituted by one or more substituent, each preferably chosen independently from the group constituted by the Cl, F, Br, I, CF_3, NO_2, OH, NH_2, CN, N_3, -OCF_3, (C_1-C_{12})alkyl, (C_1-C_{12})alkoxy, -$(CH_2)_p$-phenyl-$(X1)_q$, -NH-CO-(C_1-C_6)alkyl, -NH-C(O)O-(C_1-C_6)alkyl, -S-(C_1-C_6)alkyl, -S-phenyl-$(X1)_q$, -O-$(CH_2)_p$-phenyl-$(X1)_q$, -$(CH_2)_p$-C(O)-O-(C_1-C_6)alkyl, -$(CH_2)_p$-C(O)-(C_1-C_6)alkyl, -O-$(CH_2)_p$-NH_2, -O-$(CH_2)_p$-NH-(C_1-C_6)alkyl, -O-$(CH_2)_p$-N-di-((C_1-C_6)alkyl) and -((C_0-C_{12}))alkyl-$(X1)_q$ radicals;

X1, each time that it occurs, is independently chosen from the group constituted by the H, Cl, F, Br, I, CF_3, NO_2, OH, NH_2, CN, N_3, -OCF_3, (C_1-C_{12})alkyl, (C_1-C_{12})alkoxy, -S-(C_1-C_6)alkyl, -$(CH_2)_p$-amino, -$(CH_2)_p$-NH-(C_1-C_6)alkyl, -$(CH_2)_p$-N-di-((C_1-C_6)alkyl), -$(CH_2)_p$-phenyl and -$(CH_2)_p$-NH-(C_3-C_6)cycloalkyl radicals;

p each time that it occurs is independently 0 or an integer from 1 to 6;

q each time that it occurs is independently an integer from 1 to 5.

X represents O or S;

n represents 0 or 1; and finally

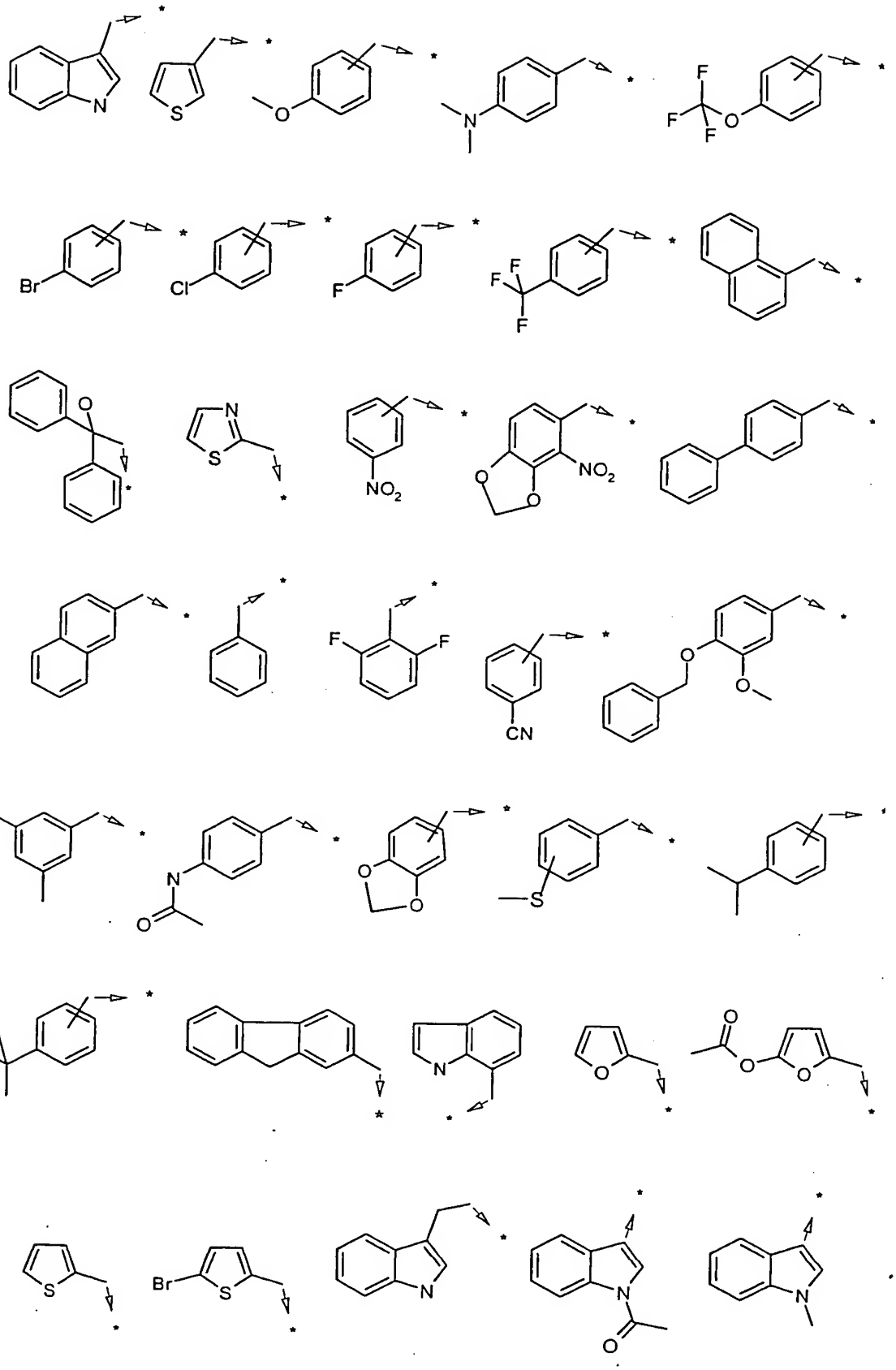
when n represents 0, m represents 1, 2 or 3, and when n represents 1, m represents 0 or 1.

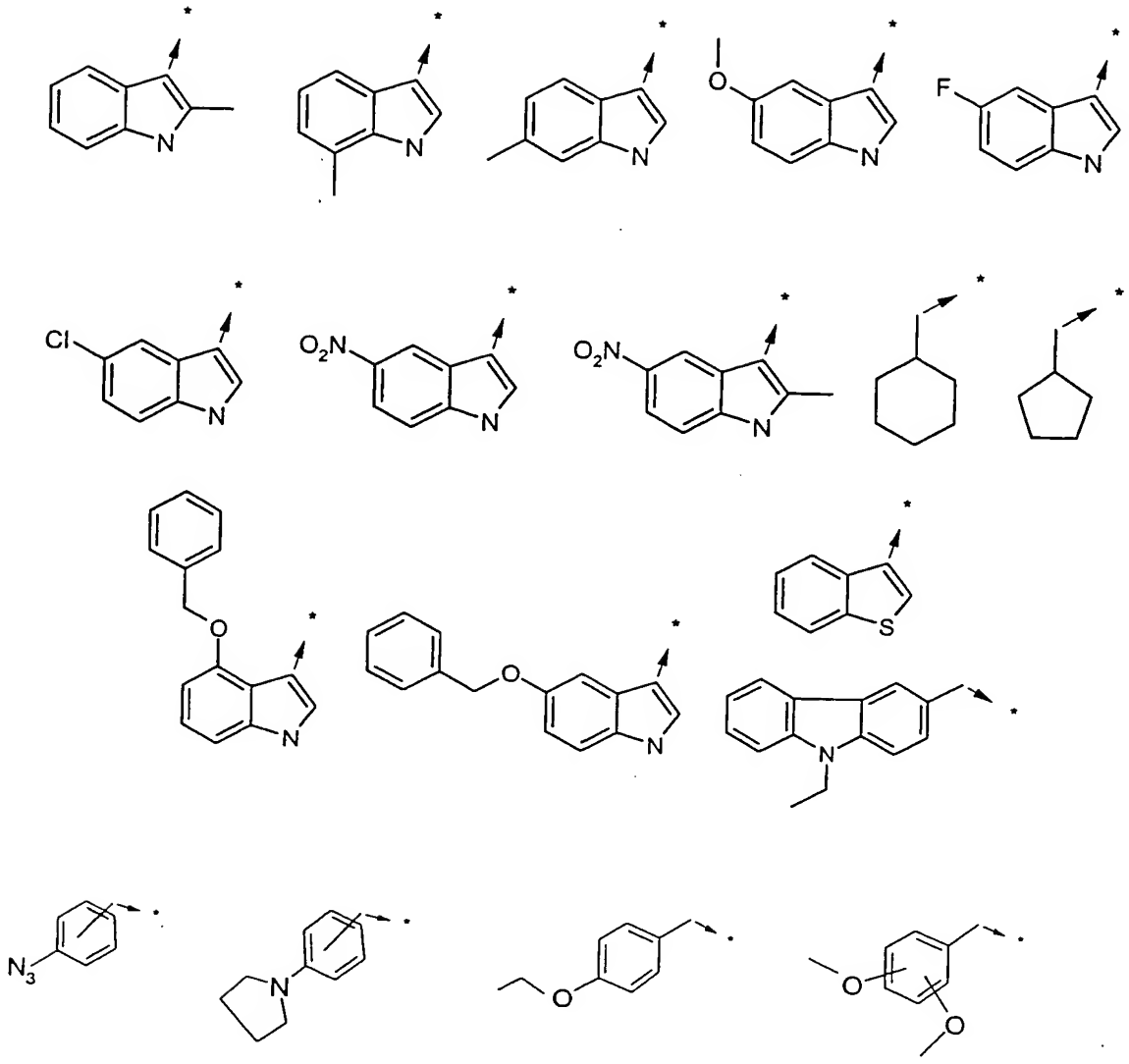
2. Compound according to claim 1, characterized in that:

R1 represents an optionally substituted aryl radical;

R2 represents H or an alkyl radical;

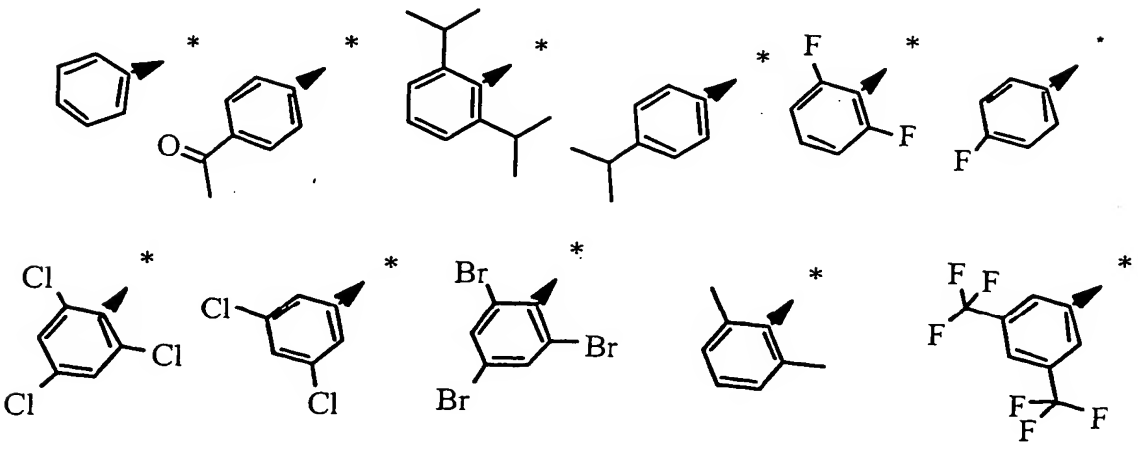
R3 represents one of the following radicals:

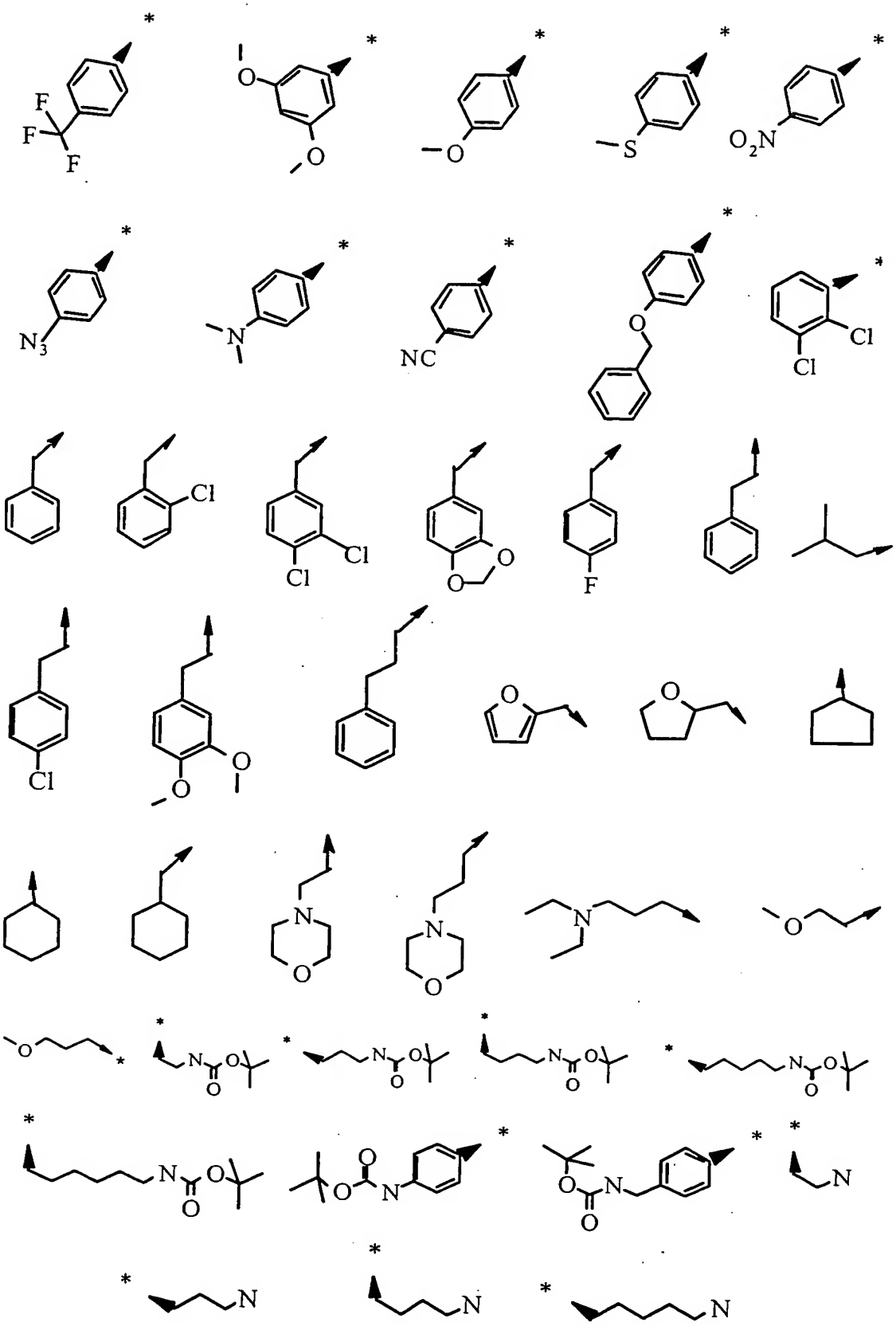


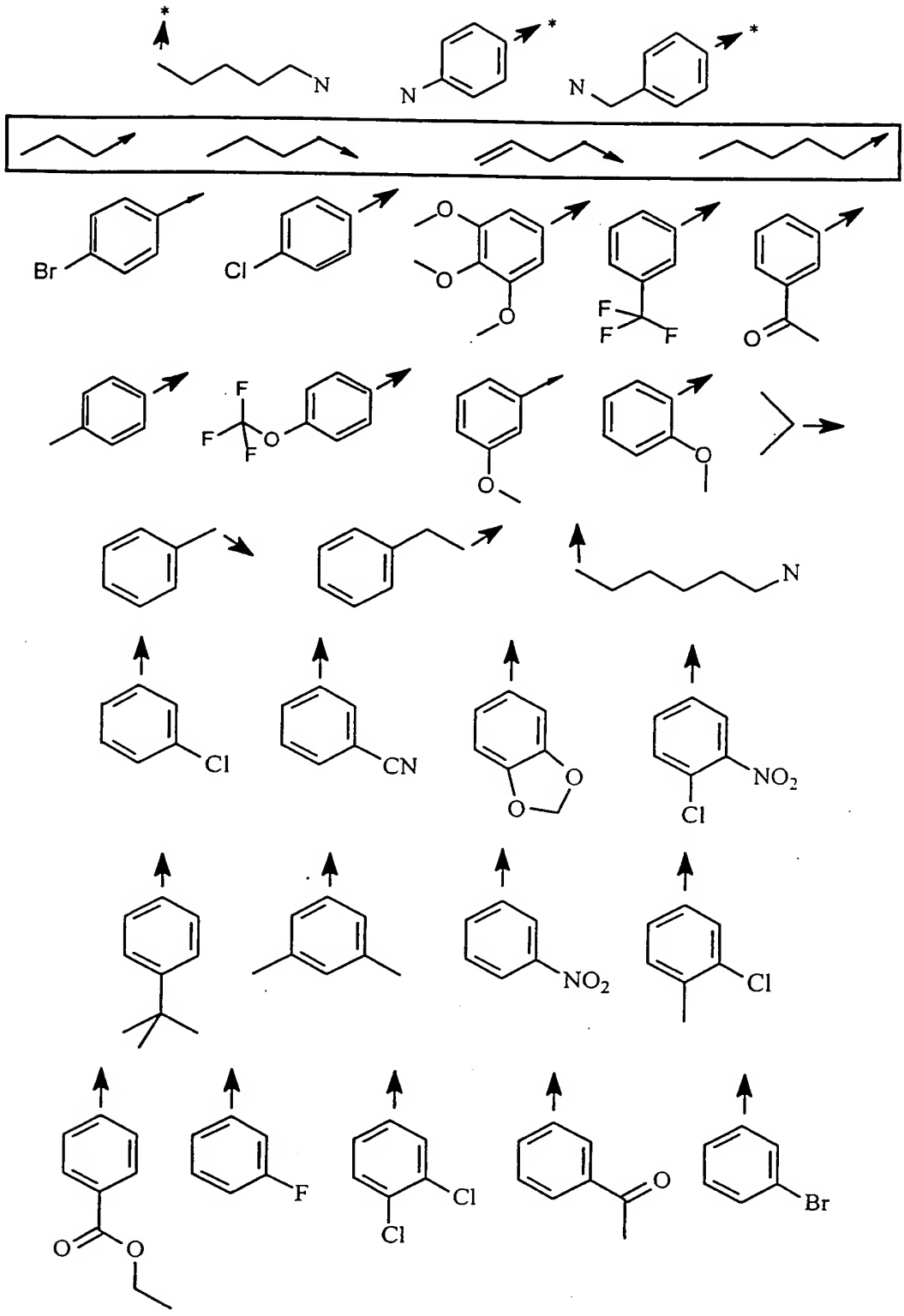


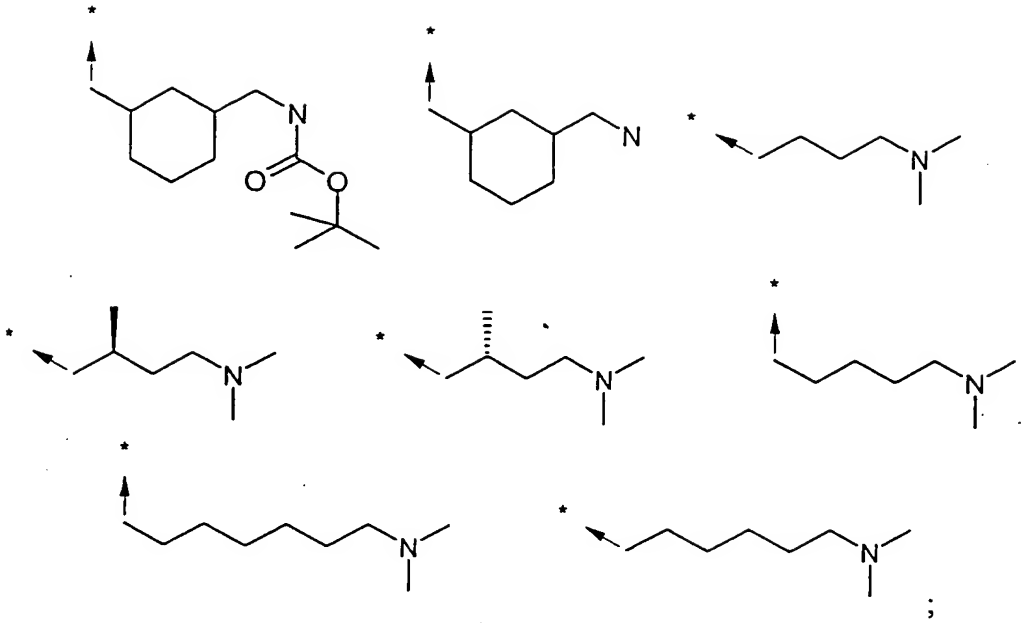
;

R4 represents one of the following radicals:






N
N
N
Br
Cl
O
O
O
F
F
F
O
F
F
O
O
O
N
Cl
CN
O
O
NO2
Cl
NO2
Cl
O
O
F
Cl
Cl
O
Br



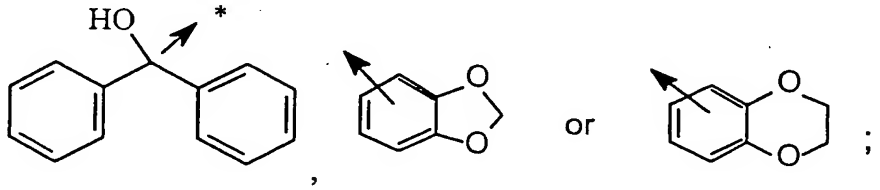
R5 represents H or an alkyl radical.

3. Compound according to claim 1, characterized in that:

R1 represents the phenyl radical optionally substituted by a halogen atom or a (C_1-C_{12})alkyl, (C_1-C_{12})alkoxy or nitro radical;

R2 and R5 represent H or alkyl;

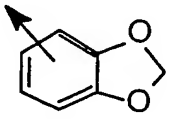
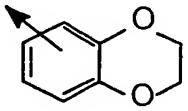
R3 represents H or $(CH_2)_p$–Z3;
Z3 represents (C_1-C_{12})alkyl, (C_3-C_8)cycloalkyl, Y1-$(CH_2)_p$-phenyl-$(X1)_n$, an optionally substituted carbocyclic or heterocyclic aryl radical, an optionally substituted heterocyclic non aromatic radical, *bis*-arylalkyl, di-arylalkyl or one of the radicals represented below



Y1 represents O, S, NH or is absent;

R4 represents $(CH_2)_p$–Z4;
Z4 represents amino, (C_3-C_8)cycloalkyl, (C_1-C_{12})alkylamino, N,N-di-(C_1-C_{12})alkylamino, amino(C_3-C_6)cycloalkyl, amino(C_1-C_6)alkyl(C_3-C_6)cycloalkyl(C_1-C_6)alkyl, carbocyclic or heterocyclic aminoaryl, an optionally substituted carbocyclic or

heterocyclic aryl radical, an optionally substituted heterocyclic non aromatic radical, *bis*-arylalkyl, di-arylalkyl or one of the radicals represented below

 or  ;

it being understood that an optionally substituted radical or an optionally substituted phenyl is optionally substituted by one or more substituent, each preferably chosen independently from the group constituted by the Cl, F, Br, I, CF_3, NO_2, OH, NH_2, CN, N_3, $-OCF_3$, (C_1-C_{12})alkyl, (C_1-C_{12})alkoxy, $-(CH_2)_p$-phenyl-$(X1)_q$, -NH-CO-(C_1-C_6)alkyl, -NH-C(O)O-(C_1-C_6)alkyl, -S-(C_1-C_6)alkyl, -S-phenyl-$(X1)_q$, -O-$(CH_2)_p$-phenyl-$(X1)_q$, $-(CH_2)_p$-C(O)-O-(C_1-C_6)alkyl, $-(CH_2)_p$-C(O)-(C_1-C_6)alkyl, -O-$(CH_2)_p$-NH_2, -O-$(CH_2)_p$-NH-(C_1-C_6)alkyl, -O-$(CH_2)_p$-N-di-$((C_1-C_6)$alkyl) and $-((C_0-C_{12}))$alkyl-$(X1)_q$ radicals;

X1, each time that it occurs, is independently chosen from the group constituted by the H, Cl, F, Br, I, CF_3, NO_2, OH, NH_2, CN, N_3, $-OCF_3$, (C_1-C_{12})alkyl, (C_1-C_{12})alkoxy, -S-(C_1-C_6)alkyl, $-(CH_2)_p$-amino, $-(CH_2)_p$-NH-(C_1-C_6)alkyl, $-(CH_2)_p$-N-di-$((C_1-C_6)$alkyl), $-(CH_2)_p$-phenyl and $-(CH_2)_p$-NH-(C_3-C_6)cycloalkyl radicals;

p each time that it occurs is independently 0 or an integer from 1 to 6; and

q each time that it occurs is independently an integer from 1 to 5.

4. Compound according to claim 3, characterized in that:

R1 represents the phenyl radical optionally substituted by a halogen atom or a (C_1-C_{12})alkyl, (C_1-C_{12})alkoxy or nitro radical;

R2 and R5 represent H or alkyl;

R3 represents $(CH_2)_p$ –Z3,
Z3 representing a (C_3-C_8)cycloalkyl radical or an optionally substituted radical chosen from the phenyl, naphthyl, furannyl, thiophene, indolyl, pyrrolyl and benzothiophene radicals;

R4 represents $(CH_2)_p$ –Z4;
Z4 represents amino, (C_1-C_{12})alkylamino, N,N-di-(C_1-C_{12})alkylamino or amino(C_1-C_6)alkyl(C_3-C_6)cycloalkyl-(C_1-C_6)alkyl;

X represents S;

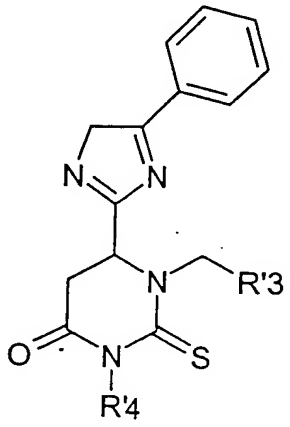
p each time that it occurs is independently 0 or an integer from 1 to 6;

m represents 0, 1 or 2; and finally

n represents 0 or 1.

5. Compound according to claim 4, characterized in that it is a compound:

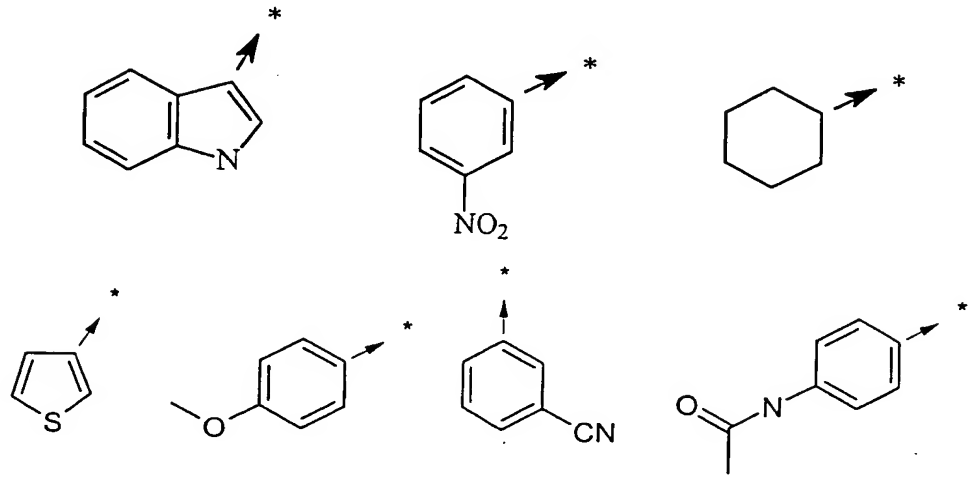
- of general sub-formula **(I)a** represented below:



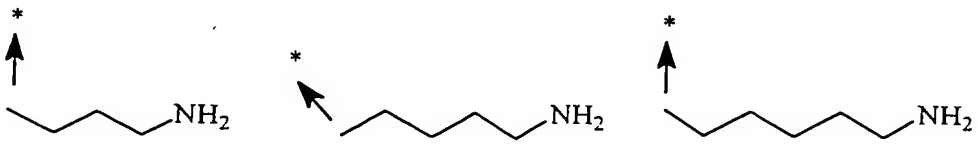
(I)a

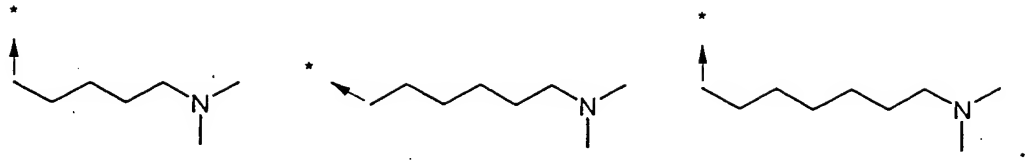
in which:

R'3 represents one of the radicals represented below:



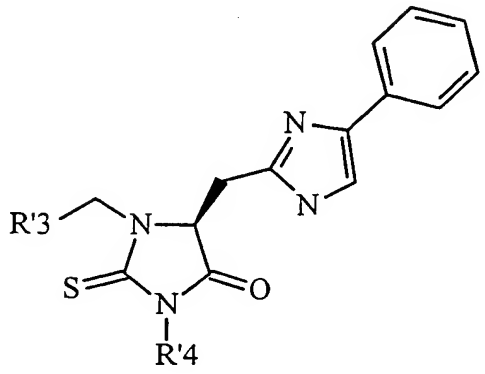
and R'4 represents one of the radicals represented below:





;

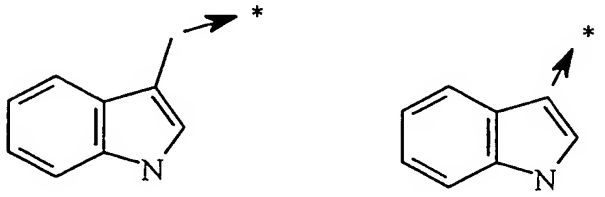
- of general sub-formula **(I)b** represented below:



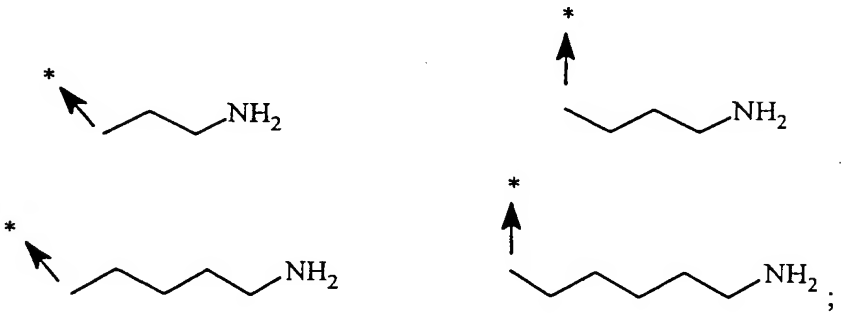
(I)b

in which:

R'3 represents one of the radicals represented below:

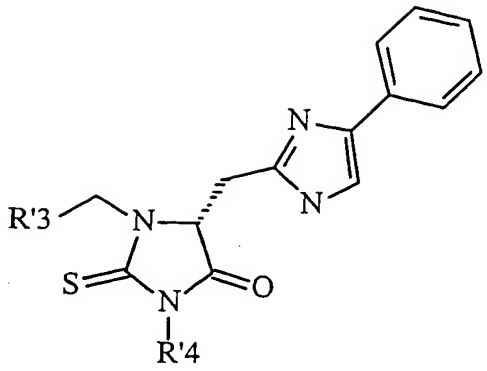


and R'4 represents one of the radicals represented below:



;

- of under-general formula **(I)c** represented below:

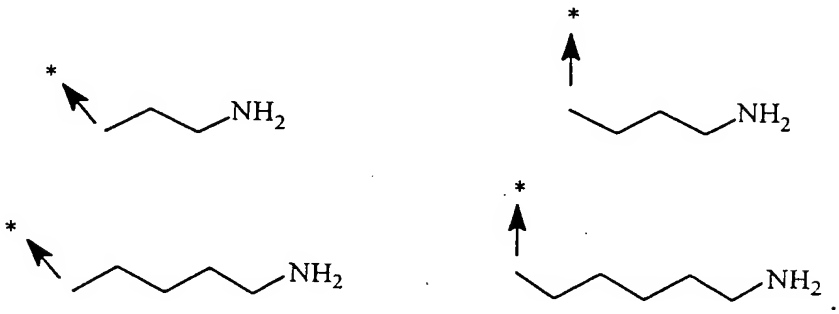


(I)c

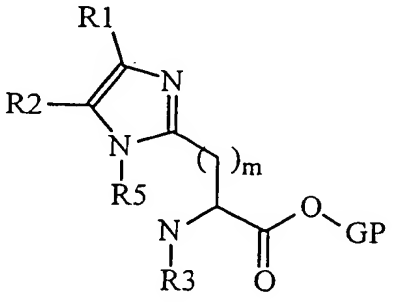
in which:

R'3 represents one of the radicals represented below:

and R'4 represents one of the radicals represented below:



6. Process for the preparation of a compound of general formula (I) according to claim 1 in which n represents 0, characterized in that the compound of general formula (II)



(II)

in which m, R1, R2, R3 and R5 have the same meaning as in general formula **(I)** of claim 1, and the O-GP radical is a parting protective group derived from an alcohol and in particular benzyloxy, methoxy or tert-butoxy, is treated in an aprotic solvent

with an isocyanate or isothiocyanate of general formula **(III)**

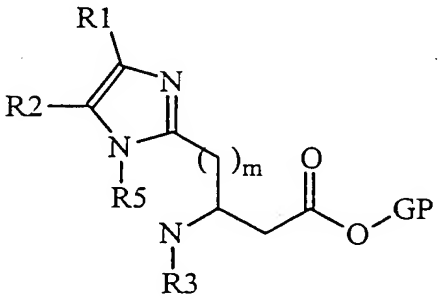
R4-N=C=X

(III)

in which R4 and X have the same meaning as in general formula **(I)** of claim 1,

preferably in the presence of a tertiary base for a duration of approximately 1 to 24 hours and at a temperature preferably comprised between 20 and 70 °C.

7. Process for the preparation of a compound of general formula **(I)** according to claim 1 in which n represents 1, characterized in that by treating in an aprotic solvent the compound of general formula **(IV)**



(IV)

in which m, R1, R2, R3 and R5 have the same meaning as in general formula **(I)** of claim 1, and the O-GP radical is a parting protective group derived from an alcohol and in particular benzyloxy, methoxy or tert-butoxy, is treated in an aprotic solvent

with an isocyanate or isothiocyanate of general formula **(III)**

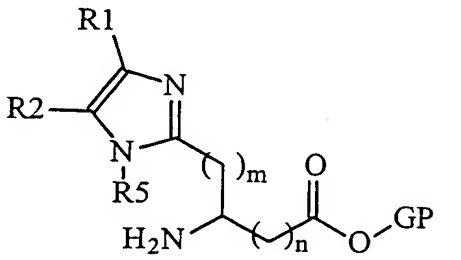
R4-N=C=X

(III)

in which R4 and X have the same meaning as in general formula **(I)** of claim 1,+

preferably in the presence of a tertiary base for a duration of approximately 1 to 48 hours and at a temperature preferably comprised between 20 and 70 °C.

8. As a new industrial compound and intermediate in the synthesis process for the compounds of general formula (I) according to claim 1, a compound of general formula (V),



(V)

in which:

R1, R2, R5, m and n have the same meaning as in general formula (I);

and the O-GP radical is a parting protective group derived from an alcohol and in particular benzyloxy, methoxy or tert-butoxy.

9. Compound according to claim 8, characterized in that it is:

- benzyl (*2S*)-2-amino-3-[(4-phenyl)-1H-imidazol-2-yl]propanoate;
- benzyl (*2R*)-2-amino-3-[(4-phenyl)-1H-imidazol-2-yl]propanoate;
- benzyl (*2S*)-2-amino-4-[(4-phenyl)-1H-imidazol-2-yl]butanoate; or
- benzyl (*2R*)-2-amino-4-[(4-phenyl)-1H-imidazol-2-yl]butanoate.

10. As a medicament, a compound according to one of claims 1 to 5 or a pharmaceutically acceptable salt of said compound.

11. Pharmaceutical composition comprising as active ingredient a compound according to one of claims 1 to 5 or a pharmaceutically acceptable salt of said compound.

12. Use of a compound according to one of claims 1 to 5 or of a pharmaceutically acceptable salt of said compound for preparing a medicament intended to treat the pathological states or diseases in which one (or more) of the somatostatin receptors are involved.

13. Use according to claim 12, characterized in that the pathological states or diseases to be treated are chosen from the group comprising the following pathological states or diseases: acromegalia, hypophyseal adenomas, Cushing's disease, gonadotrophinomas

and prolactinomas, catabolic side-effects of glucocorticoids, insulin dependent diabetes, diabetic retinopathy, diabetic nephropathy, syndrome X, dawn phenomena, angiopathy, angioplasty, hyperthyroidism, gigantism, endocrinic gastroenteropancreatic tumours including carcinoid syndrome, VIPoma, insulinoma, nesidioblastoma, hyperinsulinemia, glucagonoma, gastrinoma and Zollinger-Ellison's syndrome, GRFoma as well as acute bleeding of the esophageal varices, ulcers, gastroesophageal reflux, gastroduodenal reflux, pancreatitis, enterocutaneous and pancreatic fistulae but also diarrhoeas, refractory diarrhoeas of acquired immunodeficiency syndrome, chronic secretary diarrhoea, diarrhoea associated with irritable bowel syndrome, diarrhoeas induced by chemotherapy, disorders linked with gastrin releasing peptide, secondary pathologies with intestinal grafts, portal hypertension as well as haemorrhages of the varices in patients with cirrhosis, gastro-intestinal haemorrhage, haemorrhage of the gastroduodenal ulcer, bleeding of grafted vessels, Crohn's disease, systemic scleroses, dumping syndrome, small intestine syndrome, hypotension, scleroderma and medullar thyroid carcinoma, illnesses linked with cell hyperproliferation such as cancers and more particularly breast cancer, prostate cancer, thyroid cancer as well as pancreatic cancer and colorectal cancer, fibroses and more particularly fibrosis of the kidney, fibrosis of the liver, fibrosis of the lung, fibrosis of the skin, also fibrosis of the central nervous system as well as that of the nose and fibrosis induced by chemotherapy, and in other therapeutic fields, cephaleas including cephalea associated with hypophyseal tumours, pain, inflammatory disorders such as arthritis, panic attacks, chemotherapy, cicatrization of wounds, renal insufficiency resulting from delayed development, hyperlipidemia, obesity and delayed development linked with obesity, delayed uterine development, dysplasia of the skeleton, Noonan's syndrome, sleep apnea syndrome, Graves' disease, polycystic disease of the ovaries, pancreatic pseudocysts and ascites, leukaemia, meningioma, cancerous cachexia, inhibition of H pylori, psoriasis, chronic rejection of allografts as well as Alzheimer's disease and finally osteoporosis.

14. Use according to claim 13, characterized in that the pathological states or diseases to be treated are chosen from the group comprising the following pathological states or diseases: acromegalia, hypophyseal adenomas or endocrinic gastroenteropancreatic tumours including carcinoid syndrome, and gastrointestinal bleeding.